CANNONBALL TREE - A REVIEW

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ABSTRACT

Medicinal plants have been subject to man’s curiosity since ages. Medicinal components from plants play an important role in conventional as well as western medicine. They were the sole source of active principles capable of curing man’s ailments. Thus natural products have been a major source of drugs for centuries. Couroupita guianensis is a deciduous tree belonging to family Lecythidaceae and has a common name cannonball tree. It is native to the rainforests of Central and South America. It is cultivated in many other places. In India the tree is sacred to Hindus, who believe its hooded flowers look like the naga, and it is grown at Shiva temples. The leaves, flowers and fruits are rich in phytochemicals and are reported to contain quercitin, saponin, tryptanthrin, and many other constituents. The tree has been evaluated for many pharmacological activities such as antioxidant, antidepressant, anti-inflammatory, antifertility, anxiolytic, cytotoxic, antinociceptive, etc. Taking into consideration the medicinal properties of the tree the present review has been made to explore its phytochemical, pharmacological and other important aspects.

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INTRODUCTION
During the past decade, the indigenous or traditional systems of medicine have gained importance in the field of medicine. In most of the developing countries, large number of population still depends on traditional practitioners, who in turn are dependent on medicinal plants, to meet their primary health care needs. The World Health Organization (WHO) has estimated that about three quarters of the world’s population still relies on plant-derived medicines usually obtained from traditional healers, for their basic medicinal needs. Thus, it is clear that herbal medicine plays a pivotal role in therapeutic strategies in the modern world. One such plant that has been used widely in traditional medicine is Cannonball tree. *Couroupita guianensis* Aubl. belonging to family Lecythidaceae was first described by Fusse Aublet[1]. It is used extensively as an ingredient in many preparations which cure gastritis, scabies, bleeding piles, dysentery, scorpion poison and many. It also has rubefacient and anti rheumatic properties. It is used in ayurvedic concepts as cold relief balm and fruit pulp is used to cure headache. The flowers are used to cure cold, intestinal gas formation, stomach ache, diarrhoea, and when dried and powdered used as a snuff[2]. The fragrance of flowers is used for curing asthma and the shell of the fruit is used as utensil. The flowers also showed analgesic, anti-inflammatory[3] and immunomodulatory activity[4]. Petroleum ether and chloroform extracts of this plant exhibited larvicidal activity against vectors[5]. The main objective of this review is to give recent information along with the traditional uses of *Couroupita guianensis* which is an important tree due to its invaluable pharmacological properties. This review will help students and researchers to get the overall information about its published phytochemical and pharmacological properties for further research.

Botanical name:
*Couroupita guianensis*[1,6].

Synonym:
Cannonball tree (English), *macacareucia* (Portuguese), *coco sachapura* (Colombia, Panama), bala de canon (Costa Rica), *kanonskogelboom* (Dutch), *arbre à boulet de canon* (French), *kouroupitoumou* (French Guiana), *sala* (Indonesia), *granadillo de las huacas* (Panama), ayahuma (Peru), kailashpati (India)[6].

Scientific Classification:
Kingdom: Plantae
Division: Angiosperms
Order: Ericales
Family: Lecythideae
Genus: Couroupita
Species: *C. guianensis*

Botanical description:
The tree (figure 1) grows up to 35 meters in height. The clustered leaves (figure 2) vary in length, generally from 8 to 31 centimetres. The flowers (figure 3) are borne in large bunches up to 80 meters long. Some trees flower profusely, until the entire trunk is buried in flowers. One tree can bear 1000 flowers per day. They are strongly scented, especially at night, and in the early morning. They are large, up to 6 centimetres wide, and often brightly coloured, the six petals in shades of pink and red near the bases and yellowish toward the tips. There is a ring of stamens at the centre, and an arrangement to stamens that have been modified into a hood. The large fruit (figure 4), which is woody and very spherical, measuring up to 25 centimetres wide, gives the species the common name “cannonball tree”. A smaller fruit contains perhaps 65 seeds, while a large one can have 550. One tree can bear 150 fruits[7,8].
Figure 1: Couroupita guianensis tree

Figure 2: C. guianensis leaves

Figure 3: C. guianensis flower

Figure 4: C. guianensis fruit

Phytochemical studies

*Couroupita guianensis* leaves are rich in phytochemicals and reported to contain quercetin, saponins and tryptanthrin[9]. Isolation of tryptanthrin, indigo, indirubin, isatin, carotenoids, α, β-amyris, stigmasterol, β-sitosterol and nerol from fruits, seeds, barks, flowers have been reported earlier. The triterpenoid ester of fatty acid, β-amyrin palmitate has been isolated from the leaves of *Couroupita* guianensis[10].

![Quercetin](image)

![Tryptanthrin](image)

![Indirubin](image)

![Indigo](image)
Figure 5: Structures of major chemical constituents of *Couroupita guianensis* Aubl.

**Traditional use**
The Cannonball trees possess antibiotic, antifungal, antiseptic and analgesic properties. The parts of trees such as leaves, flowers are used to cure cold and stomach aches. Juice made from the leaves is used to cure skin diseases, and shamans of South America have even used tree parts for treating malaria. The inside of the fruit can disinfect wounds and young leaves ease toothache [11].

**Scientific reports**
Many pharmacologic studies have been conducted on *Couroupita guianensis*. A summary of these findings by various investigators is described briefly in the following sections.
Antioxidant activity
A study was carried out which reported that methanolic extract *Couroupita guianensis* (MECG) exhibited antioxidant activity. DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging assay is one of the most widely used methods for screening of antioxidant property of plant products. The methanolic extract of *Couroupita guianensis* shows good antioxidant activity in DPPH scavenging method. Percentage inhibition was found to be quite equivalent to that of the standard, ascorbic acid. IC₅₀ value of MECG in DPPH radical was found to be 39.21 and ascorbic acid used as standard was found to be 41.43. Reducing power of the extract was dose dependent which was indicated from the increase in absorbance with the increase in concentration of the extract. The findings of the present study suggested that *Couroupita guianensis* could be a potential natural source of antioxidants[12,13].

Antidepressant activity
The oral administration of the methanolic extract of *C. guianensis* was effective in producing significant antidepressant effects in the tail suspension test (TST), forced swimming test (FST) and in reserpine antagonism in mice, which showed reduction in the immobility time in mice, reduction in duration of catalepsy & degree of ptosis respectively. It showed significantly decrease in the immobility time in TST and FST, similar to that of the imipramine (10mg/kg) which served as positive control. Mice were forced to swim in a restricted space from which there was no escape, and after periods of agitation, will cease attempts to escape and become immobile. The chronic treatment of the extract significantly reduced the immobility time and increased the swimming behaviour at high dosage (500 mg/kg). This shows that the methanolic extract of the *Couroupita guianensis* possesses antidepressant activity and its specificity towards particular behavior may depend on the concentration of the extract[14-22].

Wound healing and antimicrobial activity
Proanthocyanidins and other tannins facilitate wound healing. Administration of Ethanolic extract of *Couroupita guianensis* shows decrease in the epithelialization period, along with a visibly decreased scar area. There was a significant increase in the tensile strength and hydroxyproline content compared to the control group and comparable to the nitrofurazone group. The observations and results indicate that the alcoholic extract of *Couroupita guianensis* significantly stimulated wound contraction. Ethanolic extract also exhibited a potential inhibitory effect on all the pathogens examined, in the following order, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Ecsertia coli* minimum inhibitory concentration (MIC) being 0.56, 0.78, 0.89, 1.33 mg/ ml, respectively. Erythromycin and tetracycline were used as standards. The 50% aqueous ethanol served as a negative control and showed no inhibiting effect. The significant antimicrobial effect of ethanolic extract of *C. guianensis* against all the four pathogens confirmed that the compounds present in the crude extract are responsible for the effective antimicrobial activity[23,24].

Antifungal activity
The antifungal activity of the isolated phytochemical fractions namely alkaloid, phenolic and flavonoid fractions were determined. The fungal strains *Candida albicans*, *Aspergillus fumigatus* and *Aspergillus flavus* were inhibited by more than 50% by the alkaloid fractions of the leaves, flower and fruit pulp of *Couroupita guianensis*. The phenolic and flavonoid fractions of *Couroupita guianensis* did not show prominent inhibition of the fungal species. Hence it is evident that the antifungal property of the plant is predominantly due to only the alkaloid compounds[25].

Antulcer activity
The ethanolic extract of *Couroupita guianensis* shows protection against gastric lesions in the experimental rats, reduced gastric volume, free acidity, total acidity and ulcer index thus showing the anti-secretary mechanism involved in the extracts for their anti-ulcerogenic activity. The protection by ethanolic extract against characteristic lesions may be due to both reductions in gastric acid secretion and gastric cytoprotection or enhancement of the mucosal barrier through the increase production of prostaglandin. This property may be due to the presence of glycosides in the ethanolic extract. Further studies are needed for their exact mechanism of action on gastric acid secretion and gastric cytoprotection[26-30].

Immunomodulatory activity
Various extracts such as methanol, ethanol and hexane of the flowers of *Couroupita guianensis* were evaluated for potential immunomodulatory activity using the *in vitro* polymorphonuclear leukocyte function test (human neutrophils). The methanolic extract was evaluated for immunomodulatory activity *in vivo* studies, using rats as the animal model. The extracts were tested for hypersensitivity and hemagglutination reactions, using sheep red blood cells (SRBC) as the antigen. Distilled water served as a control in all the tests. The successive methanol and water extracts exhibited a significant increase in the percentage phagocytosis versus the control. In the *in vivo* studies, the successive methanolic extract was found to exhibit a dose related increase in the hypersensitivity reaction, to the SRBC antigen at concentration of 100 and 200 mg/kg in animal studies. The successive methanol extract was found to
stimulate cell mediated and antibody mediated immune responses in rats. It also enhanced the phagocytic function of the human neutrophils, *in vivo*[31].

**Cytotoxic activity**
The methanolic extract of the dried flower of *Couroupita guianensis* was screened for cytotoxicity against the HeLa, NIH 3T3 and HepG2 cancer cell lines and showed significant IC$_{50}$ values of 202.6, 280 and 470.8 µg/ml respectively[32].

**Anxiolytic activity**
*Couroupita guianensis* has rich source of triterpenoids which have been concerned with anxiolytic activity. The methanolic extract of *Couroupita guianensis* root was administered orally in a dose range of 125, 250 and 500 mg/kg of the body weight of mice. The anxiolytic activity was evaluated using light and dark model (LDM), elevated plus maze (EPM) and hole board test (HBT) in mice. Results of the activity showed significantly increase in number of entries in light room in LDM. In EPM there was significant increase in number of entries and time spent in open arm in dose dependent manner, similar to that of the diazepam (3 mg/kg) which served as a positive control. Also, it was observed that in HBT there is increase in number of head dipping as compared to normal vehicle control. The significance of difference among the various treated groups and control group were analyzed by means of one-way analysis of variance (ANOVA) followed by Dunnett’s tests. In conclusion, methanolic extract of *Couroupita guianensis* root possess potential anxiolytic activity (through its action on GABA or benzodiazepine receptors)) and has therapeutic potential in the treatment of CNS disorders and provides evidence at least at a preclinical level[33].

**Analgesic and anti-inflammatory activity**
Analgesic activity was evaluated using tail flick method and anti-inflammatory activity was screened by measuring the reduction in carrageenan induced hind paw oedema. The potency of various extracts of flower and bark such as methanol, ethanol, hexane were compared with paracetamol (200 mg/kg) for analgesic and indomethacin (10 mg/kg) for anti-inflammatory activities. All the extracts of *C. guianensis* showed analgesic and anti-inflammatory activity. The peak analgesic effect of flower was seen after 1 hr while bark extracts showed peak effect after 2 hrs. Maximum reduction in inflammation by the extracts was observed after 3 hrs. *C. guianensis* is almost equipotent to paracetamol in its analgesic activity and to indomethacin in its anti-inflammatory activity[34].

**Antifertility activity**
Antifertility activity of benzene, ethanol and water extracts of bark and flowers of *C. guianensis* was studied for their effect on duration of various stages of oestrus cycle in adult female rats and on the number implantation sites in the pregnant rats. All the ethanol and water extracts of *C. guianensis* bark and flower showed significant prolongation of dioestrus stage ($p<0.05$). Ethanol extract of *C. guianensis* bark and all the extracts of its flower reduced the number of implantations. The disturbances in the reproductive cycle indicate effect of the plant on the sex hormones in the animals. Prevention of implantation may be due their interference in the receptive stage of the uteri and endometrial sensitivity for decidualisation[35].

**Anthelmentic activity**
The anthelmentic potential of *C. guianensis* has been evaluated. *Pheritima posthuma* was divided into ten groups. Each group consists of six earth worms of same type and treated with the following. 50 ml of test solution containing 20, 50 and 100 mg/ml of test extracts (Chloroform, acetone and ethanol extracts of flowers of *Couroupita guianensis*) and piperazine citrate (10mg/kg). The Mean time of paralysis and death was recorded in minutes. The paralysis time was recorded when no movement of any sort could be observed except when the worms were shaken vigorously. Time for death of worms was recorded when worms were neither moved while shaken vigorously nor when dipped in warm water (50 °C). Chloroform, acetone and ethanol extracts of flowers of *C. guianensis* showed significant anthelmentic activity at the concentration 50 mg/ml and 100 mg/ml against *Pheritima posthuma*. Activity was found to be increased with dose (shortest time of paralysis and death was observed at 100 mg/ml) and the activity was comparable to the well known anthelmentic agent Piperazine citrate[36].

**Protective effect against oxygen reactive species and skin fibroblast stimulation**
Hydroalcoholic leaf extracts of *Couroupita guianensis* were examined for antioxidant activity, phytochemical and total phenolic composition, stimulation of human skin fibroblast (HSF) proliferation and UV-absorption. The radical scavenging capacity, reducing power and protection against joint oxidation of linoleic acid and β-carotene bleaching oxidation in emulsion were used to evaluate the antioxidant activity. The *in vitro* antioxidant activity may be due to the presence of a high total phenolic content. Active principles of the extracts are the flavonoids, 2′,4′-dihydroxy-6′-methoxy-3′,5′-dimethylchalcone,7-hydroxy-5-methoxy-6,8-dimethylflavanone and the phenolic acid 4-hydroxybenzoic acid. In addition, a high level of stimulation of HSF proliferation and significant absorption of
UV radiation are also observed. The results suggest that the hydroalcoholic leaf extracts of *C. guianensis* have promising skin care properties [37].

**Insecticidal and pesticidal properties**

Insect pests play a major role in damaging the crops and hence there is a need to use efficacious control agents. More than 2,000 species of plants are known to possess insecticidal properties. Methanol extract derived fractions of *C. guianensis* inhibited the growth of microorganisms. Petroleum ether and chloroform extracts of this plant exhibited larvicidal activity against vectors. The antifeedant and larvicidal activities of *C. guianensis* against the notorious agricultural pest, *H. Armigera* has been studied. Maximum feeding deterency (81.67 %) and least LC$_{50}$ (2.72 %) for larval mortality were seen in hexane extract. Hexane extract was subjected to column chromatography using different ratio of hexane-ethyl acetate solvent system. Totally eight fractions were collected. The fractions were screened at 125, 250, 500 and 1,000 mg/kg concentrations against *H. armigera* using no-choice leaf disc method. Fraction eight showed maximum antifeedant (86.24 %) and larvicidal (80.88 %) activities at 1,000 mg/kg concentration. *C. guianensis* could be utilized in pest control programme[38].

**Antinociceptive activity**

Crude ethanolic extract (CEE) of *C. guianensis* and its dichloromethane, ethyl acetate and hexane fractions significantly inhibited the number of contortions induced by acetic acid. All fractions showed antinociceptive activity in the tail flick model, the hexane and ethyl acetate being the most potent and long acting fractions. In the hot plate method the highest effect observed was at the dose of 100mg/kg from all fractions. Administration of naloxone (opioid receptor antagonist) inhibited the antinociceptive effect of fractions. Pre-treatment of mice with atropine (muscarinic receptor antagonist) reduced the antinociceptive activity of crude ethanolic extract and its fractions, the exception being the dichloromethane fraction. Mecamylamine (nicotinic receptor antagonist) did not inhibit the effect of dichloromethane fraction. L-nitro arginine methyl ester (nitric oxide synthase inhibitor) reduced the anti-hyperalgesic effect of all fractions, but the most prominent effect was observed in the antinociceptive activity caused by CEE and butanol fraction. Results obtained demonstrated that *Couroupita guianensis* CEE and its fractions have antinociceptive activity that is mediated, at least in part, by opioid and cholinergic systems and nitric oxide pathway[39].

**CONCLUSION**

The extensive literature survey revealed that *Couroupita guianensis* is an important medicinal plant with diverse pharmacological spectrum. The plant shows the presence of many chemical constituents which are responsible for varied pharmacological and medicinal properties such as antidepressant, antioxidant, antimicrobial, antifertility, anthelmeitic, etc. The evaluation needs to be carried out on *Couroupita guianensis* in order to use it in formulations of the plant and their practical clinical applications, which can be used for the welfare of the mankind.

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List of abbreviations:

MECG: Methanolic extract C. guianensis
DPPH: 1, 1-diphenyl-2-picrylhydrazyl
TST: Tail suspension test
FST: Forced swimming test
MIC: Minimum inhibitory concentration
SRBC: Sheep red blood cells
IC_{50}: Half maximal inhibitory concentration
LDM: light and dark model
EPM: elevated plus maze
HBT: Hole board test
ANOVA: One-way analysis of variance
HSF: Human skin fibroblast
CEE: Crude ethanolic extract

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